

-1-

SEQUENCE LISTING

<110> Gardella, Thomas J.
Kronenberg, Henry M.
Potts, John T.

<120> Conformationally Constrained Parathyroid Hormone (PTH) Analogs
With Lactam Bridges

<130> 0609.514PC00

<160> 37

<170> PatentIn version 3.2

<210> 1
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutated hPTH

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa can represent Gly, Ser, Ala or alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa can represent Ala, Ser, alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa can represent Asp, Glu or Lys

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Xaa can represent Asp, Glu or Lys

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa can represent Arg, Leu or Homoarginine

<220>
<221> MISC_FEATURE
<222> (12)..(12)
<223> Xaa can represent Ala or Gly

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa can represent Trp or His

<220>
<221> MOD_RES
<222> (14)..(14)
<223> AMIDATION

-2-

<400> 1

Xaa Val Xaa Glu Ile Xaa Leu Met His Xaa Xaa Xaa Lys Xaa
1 5 10

<210> 2

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Mutated hPTH

<220>

<221> MISC_FEATURE

<222> (6)..(6)

<223> Xaa can represent Asp, Glu or Lys

<220>

<221> MISC_FEATURE

<222> (9)..(9)

<223> Xaa represents homoarginine

<220>

<221> MOD_RES

<222> (12)..(12)

<223> AMIDATION

<400> 2

Ala Val Ala Glu Ile Xaa Leu Met Xaa Ala Lys Trp
1 5 10

<210> 3

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> [(Glu-6, Lys-10)lac.]PTH(1-14)

<220>

<221> MISC_FEATURE

<222> (1)..(14)

<223> Sequence is cyclized via a 6-10 lactam bridge

<220>

<221> MISC_FEATURE

<222> (11)..(11)

<223> Xaa represents homoarginine

<220>

<221> MOD_RES

<222> (14)..(14)

<223> AMIDATION

<400> 3

-3-

Ala Val Ala Glu Ile Glu Leu Met His Lys Xaa Ala Lys Trp
 1 5 10

<210> 4
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> [(Lys-6, Lys-10)lac.]PTH(1-14)

<220>
 <221> MISC_FEATURE
 <222> (1)..(14)
 <223> Sequence is cyclized via 6-10 lactam bridge

<220>
 <221> MOD_RES
 <222> (14)..(14)
 <223> AMIDATION

<400> 4

Ala Val Ala Glu Ile Lys Leu Met His Lys Xaa Ala Lys Trp
 1 5 10

<210> 5
 <211> 34
 <212> PRT
 <213> Rattus sp.

<220>
 <221> MOD_RES
 <222> (34)..(34)
 <223> AMIDATION

<400> 5

Ala Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Lys His Leu Ala
 1 5 10 15

Ser Val Glu Arg Met Gln Trp Leu Arg Lys Lys Leu Gln Asp Val His
 20 25 30

Asn Phe

<210> 6
 <211> 34
 <212> PRT
 <213> Homo sapiens

<220>
 <221> MOD_RES

-4-

<222> (34)..(34)
 <223> AMIDATION

<400> 6

Ser Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Lys His Leu Asn
 1 5 10 15

Ser Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His
 20 25 30

Asn Phe

<210> 7
 <211> 34
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mutated hPTH

<220>
 <221> MISC_FEATURE
 <222> (6)..(6)
 <223> Xaa can represent Ala, Glu or Gln

<220>
 <221> MISC_FEATURE
 <222> (10)..(10)
 <223> Xaa can represent Ala, Glu or Gln

<220>
 <221> MOD_RES
 <222> (34)..(34)
 <223> AMIDATION

<400> 7

Ser Val Ser Glu Ile Xaa Leu Met His Xaa Leu Gly Lys His Leu Asn
 1 5 10 15

Ser Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His
 20 25 30

Asn Tyr

<210> 8
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mutated hPTH(1-11)

-5-

<220>
<221> MOD_RES
<222> (11)..(11)
<223> AMIDATION

<400> 8

Ala Val Ala Glu Ile Gln Leu Met His Gln Arg
1 5 10

<210> 9
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> [Aib-1,3]PTH(1-14)

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa represents alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa represents alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (14)..(14)
<223> AMIDATION

<400> 9

Xaa Val Xaa Glu Ile Gln Leu Met His Gln Xaa Ala Lys Trp
1 5 10

<210> 10
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ([Tyr-34]hPTH(1-34)amide)

<220>
<221> MOD_RES
<222> (34)..(34)
<223> AMIDATION

<400> 10

-6-

Ser Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Lys His Leu Asn
 1 5 10 15

Ser Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His
 20 25 30

Asn Tyr

<210> 11
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> [Ala-1,3,12, Gln-10, Har-11, Trp-14]PTH(1-14)amide

<220>
 <221> MISC_FEATURE
 <222> (11)..(11)
 <223> Xaa represents homoarginine

<220>
 <221> MOD_RES
 <222> (14)..(14)
 <223> AMIDATION

<400> 11

Ala Val Ala Glu Ile Gln Leu Met His Gln Xaa Ala Lys Trp
 1 5 10

<210> 12
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> [Ala-1,3, Gln-10, Har-11]PTH(1-11)amide

<220>
 <221> MISC_FEATURE
 <222> (11)..(11)
 <223> Xaa represents homoarginine

<220>
 <221> MOD_RES
 <222> (11)..(11)
 <223> AMIDATION

<400> 12

Ala Val Ala Glu Ile Gln Leu Met His Gln Xaa
 1 5 10

-7-

<210> 13
<211> 84
<212> PRT
<213> Homo sapiens

<220>
<221> MOD_RES
<222> (84)..(84)
<223> AMIDATION

<400> 13

Ser Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Lys His Leu Asn
1 5 10 15

Ser Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His
20 25 30

Asn Phe Val Ala Leu Gly Ala Pro Leu Ala Pro Arg Asp Ala Gly Ser
35 40 45

Gln Arg Pro Arg Lys Lys Glu Asp Asn Val Leu Val Glu Ser His Glu
50 55 60

Lys Ser Leu Gly Glu Ala Asp Lys Ala Asp Val Asn Val Leu Thr Lys
65 70 75 80

Ala Lys Ser Gln

<210> 14
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> [M] PTH(1-21)

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (21)..(21)
<223> AMIDATION

<400> 14

Ala Val Ala Glu Ile Gln Leu Met His Gln Xaa Ala Lys Trp Leu Asn
1 5 10 15

-8-

Ser Met Glu Arg Val
20

<210> 15
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> [Aib-1,3, M]PTH(1-21)

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa represents alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa represents alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (21)..(21)
<223> AMIDATION

<400> 15

Xaa Val Xaa Glu Ile Gln Leu Met His Gln Xaa Ala Lys Trp Leu Asn
1 5 10 15

Ser Met Glu Arg Val
20

<210> 16
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> [M]PTH(1-21) radiolabeled with Iodine isotope 125

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (21)..(21)
<223> AMIDATION

-9-

<400> 16

Ala Val Ala Glu Ile Gln Leu Met His Gln Xaa Ala Lys Trp Leu Asn
1 5 10 15

Ser Met Glu Arg Val
20

<210> 17

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> [Aib-1,3, M]PTH(1-21) radiolabeled with Iodine isotope 125

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa represents alpha-aminoisobutyric acid

<220>

<221> MISC_FEATURE

<222> (3)..(3)

<223> Xaa represents alpha-aminoisobutyric acid

<220>

<221> MISC_FEATURE

<222> (11)..(11)

<223> Xaa represents homoarginine

<220>

<221> MOD_RES

<222> (21)..(21)

<223> AMIDATION

<400> 17

Xaa Val Xaa Glu Ile Gln Leu Met His Gln Xaa Ala Lys Trp Leu Asn
1 5 10 15

Ser Met Glu Arg Val
20

<210> 18

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> [Ala-6]PTH(1-11)

<220>

<221> MOD_RES

<222> (11)..(11)

<223> AMIDATION

-10-

<400> 18

Ala Val Ala Glu Ile Ala Leu Met His Gln Arg
1 5 10

<210> 19

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> [Ala-10]PTH(1-11)

<220>

<221> MOD_RES

<222> (11)..(11)

<223> AMIDATION

<400> 19

Ala Val Ala Glu Ile Gln Leu Met His Ala Arg
1 5 10

<210> 20

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> [Ala-6,10]PTH(1-11)

<220>

<221> MOD_RES

<222> (11)..(11)

<223> AMIDATION

<400> 20

Ala Val Ala Glu Ile Ala Leu Met His Ala Arg
1 5 10

<210> 21

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> [Ala-6, Aib-1,3]PTH(1-14)

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa represents alpha-aminoisobutyric acid

<220>

<221> MISC_FEATURE

-11-

<222> (3)..(3)
<223> Xaa represents alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (14)..(14)
<223> AMIDATION

<400> 21

Xaa Val Xaa Glu Ile Ala Leu Met His Gln Xaa Ala Lys Trp
1 5 10

<210> 22
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> [Aib-1,3, Ala-10]PTH(1-14)

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa represents alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa represents alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (14)..(14)
<223> AMIDATION

<400> 22

Xaa Val Xaa Glu Ile Gln Leu Met His Ala Xaa Ala Lys Trp
1 5 10

<210> 23
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> [Aib-1,3, Ala-6,10]PTH(1-14)

-12-

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa represents alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa represents alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (14)..(14)
<223> AMIDATION

<400> 23

Xaa Val Xaa Glu Ile Ala Leu Met His Ala Xaa Ala Lys Trp
1 5 10

<210> 24
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> [Glu-6, Lys-10]PTH(1-14) (linear)

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (14)..(14)
<223> AMIDATION

<400> 24

Ala Val Ala Glu Ile Glu Leu Met His Lys Xaa Ala Lys Trp
1 5 10

<210> 25
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> [Lys-6, Glu-10]PTH(1-14) (linear)

<220>
<221> MISC_FEATURE

-13-

<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (14)..(14)
<223> AMIDATION

<400> 25

Ala Val Ala Glu Ile Lys Leu Met His Glu Xaa Ala Lys Trp
1 5 10

<210> 26
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> [(Lys-6, Glu-10)lac.]PTH(1-14)

<220>
<221> MISC_FEATURE
<222> (1)..(14)
<223> Sequence is cyclized via a 6-10 lactam bridge

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (14)..(14)
<223> AMIDATION

<400> 26

Ala Val Ala Glu Ile Lys Leu Met His Glu Xaa Ala Lys Trp
1 5 10

<210> 27
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> [Ala-6,10]PTH(1-34)

<220>
<221> MOD_RES
<222> (34)..(34)
<223> AMIDATION

<400> 27

Ser Val Ser Glu Ile Ala Leu Met His Ala Leu Gly Lys His Leu Asn
1 5 10 15

-14-

Ser Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His
20 25 30

Asn Tyr

<210> 28
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> [Ala-6,10]PTH(1-34)

<220>
<221> MOD_RES
<222> (34)..(34)
<223> AMIDATION

<400> 28

Ser Val Ser Glu Ile Ala Leu Met His Asn Leu Gly Lys His Leu Asn
1 5 10 15

Ser Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His
20 25 30

Asn Tyr

<210> 29
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> [Ala-10]PTH(1-34)

<220>
<221> MOD_RES
<222> (34)..(34)
<223> AMIDATION

<400> 29

Ser Val Ser Glu Ile Gln Leu Met His Ala Leu Gly Lys His Leu Asn
1 5 10 15

Ser Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His
20 25 30

Asn Tyr

-15-

<210> 30
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> [Ala-3,12, Gln-10, Har-11, Trp-14, Arg-19, Tyr-21]PTH(1-21)amide
radiolabeled with Iodine isotope 125

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa represents homoarginine

<220>
<221> MOD_RES
<222> (21)..(21)
<223> AMIDATION

<400> 30

Ser Val Ala Glu Ile Gln Leu Met His Gln Xaa Ala Lys Trp Leu Asn
1 5 10 15

Ser Met Arg Arg Tyr
20

<210> 31
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutated hPTH(1-34)

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa can represent Gly, Ser, Ala or alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa can represent Ser, Ala or alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa can represent Asp, Glu or Lys

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Xaa can represent Asp, Glu or Lys

-16-

<220>
 <221> MISC_FEATURE
 <222> (11)..(11)
 <223> Xaa can represent Arg, Har or Leu

<220>
 <221> MISC_FEATURE
 <222> (12)..(12)
 <223> Xaa can represent Ala or Gly

<220>
 <221> MISC_FEATURE
 <222> (14)..(14)
 <223> Xaa can represent Trp or His

<220>
 <221> MOD_RES
 <222> (14)..(14)
 <223> AMIDATION

<400> 31

Xaa	Val	Xaa	Glu	Ile	Xaa	Leu	Met	His	Xaa	Xaa	Xaa	Lys	Xaa	Leu	Asn
1				5					10					15	

Ser	Met	Glu	Arg	Val	Glu	Trp	Leu	Arg	Lys	Lys	Leu	Gln	Asp	Val	His
			20					25					30		

Asn Tyr

<210> 32
 <211> 21
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mutated hPTH(1-21)

<220>
 <221> MISC_FEATURE
 <222> (1)..(1)
 <223> Xaa can represent Gly, Ser, Ala or alpha-aminoisobutyric acid

<220>
 <221> MISC_FEATURE
 <222> (3)..(3)
 <223> Xaa can represent Ser, Ala or alpha-aminoisobutyric acid

<220>
 <221> MISC_FEATURE
 <222> (6)..(6)
 <223> Xaa can represent Asp, Glu or Lys

<220>
 <221> MISC_FEATURE
 <222> (10)..(10)
 <223> Xaa can represent Asp, Glu or Lys

-17-

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa can represent Arg, Har or Leu

<220>
<221> MISC_FEATURE
<222> (12)..(12)
<223> Xaa can represent Ala or Gly

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa can represent Trp or His

<220>
<221> MOD_RES
<222> (14)..(14)
<223> AMIDATION

<400> 32

Xaa	Val	Xaa	Glu	Ile	Xaa	Leu	Met	His	Xaa	Xaa	Xaa	Lys	Xaa	Leu	Asn
1				5					10					15	

Ser Met Glu Arg Val
20

<210> 33
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutated hPTH(1-13)

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa can represent Gly, Ser, Ala or alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa can represent Ser, Ala or alpha-aminoisobutyric acid

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa can represent Asp, Glu or Lys

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Xaa can represent Asp, Glu or Lys

<220>
<221> MISC_FEATURE
<222> (11)..(11)

-18-

<223> Xaa can represent Arg, Har or Leu

<220>

<221> MISC_FEATURE

<222> (12)..(12)

<223> Xaa can represent Ala or Gly

<220>

<221> MOD_RES

<222> (13)..(13)

<223> AMIDATION

<400> 33

Xaa Val Xaa Glu Ile Xaa Leu Met His Xaa Xaa Xaa Lys
1 5 10

<210> 34

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Mutated hPTH(1-12)

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa can represent Gly, Ser, Ala or alpha-aminoisobutyric acid

<220>

<221> MISC_FEATURE

<222> (3)..(3)

<223> Xaa can represent Ser, Ala or alpha-aminoisobutyric acid

<220>

<221> MISC_FEATURE

<222> (6)..(6)

<223> Xaa can represent Asp, Glu or Lys

<220>

<221> MISC_FEATURE

<222> (10)..(10)

<223> Xaa can represent Asp, Glu or Lys

<220>

<221> MISC_FEATURE

<222> (11)..(11)

<223> Xaa can represent Arg, Har or Leu

<220>

<221> MISC_FEATURE

<222> (12)..(12)

<223> Xaa can represent Ala or Gly

<220>

<221> MOD_RES

<222> (12)..(12)

<223> AMIDATION

-19-

<400> 34

Xaa Val Xaa Glu Ile Xaa Leu Met His Xaa Xaa Xaa
1 5 10

<210> 35

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mutated hPTH(1-11)

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa can represent Gly, Ser, Ala or alpha-aminoisobutyric acid

<220>

<221> MISC_FEATURE

<222> (3)..(3)

<223> Xaa can represent Ser, Ala or alpha-aminoisobutyric acid

<220>

<221> MISC_FEATURE

<222> (6)..(6)

<223> Xaa can represent Asp, Glu or Lys

<220>

<221> MISC_FEATURE

<222> (10)..(10)

<223> Xaa can represent Asp, Glu or Lys

<220>

<221> MISC_FEATURE

<222> (11)..(11)

<223> Xaa can represent Arg, Har or Leu

<220>

<221> MOD_RES

<222> (11)..(11)

<223> AMIDATION

<400> 35

Xaa Val Xaa Glu Ile Xaa Leu Met His Xaa Xaa
1 5 10

<210> 36

<211> 14

<212> PRT

<213> Homo sapiens

<220>

<221> MOD_RES

<222> (14)..(14)

<223> AMIDATION

-20-

<400> 36

Ser	Val	Ser	Glu	Ile	Gln	Leu	Met	His	Asn	Leu	Gly	Lys	His
1				5					10				

<210> 37

<211> 14

<212> PRT

<213> Rattus sp.

<220>

<221> MOD_RES

<222> (14)..(14)

<223> AMIDATION

<400> 37

Ala	Val	Ser	Glu	Ile	Gln	Leu	Met	His	Asn	Leu	Gly	Lys	His
1				5					10				